Decision Summary

Based on our review of the evidence as a whole, the previous coverage decision, and in light of the general absence of studies evaluating the impact of using TEB for managing patients with cardiac disease, we conclude that TEB continues to be reasonable and necessary for the following indications with minor modifications to meet the current literature and guidelines:

- Differentiation of cardiogenic from pulmonary causes of acute dyspnea when physician history, physical examination, and standard assessment tools provide insufficient information and the treating physician has determined that TEB hemodynamic data are necessary for appropriate management of the patient;

- Optimization of atrioventricular interval for patients with an atrioventricular sequential pacemaker when physician history, physical examination, and standard assessment tools provide insufficient information and the treating physician has determined that TEB hemodynamic data are necessary for appropriate management of the patient; and

- Monitoring of *continuous* inotropic therapy for patients with terminal congestive heart failure, when those patients have chosen to die with comfort at home, or in patients waiting at home for a heart transplant;

- Evaluation for rejection in patients with a heart transplant as a predetermined alternative to a myocardial biopsy. Medical necessity would need to be documented should a biopsy be performed after TEB.

- Optimization of fluid management in patients with congestive heart failure when physician history, physical examination, and standard assessment tools provide insufficient information and the treating physician has determined that TEB hemodynamic data are necessary for appropriate management of the patient;

Under our original national policy, coverage of TEB for the management of hypertension could have been inferred under the broad category of “suspected or known cardiovascular disease,” and therefore, discretionarily covered by some Medicare contractors if so interpreted. No evidence to support this use was presented in connection with the original coverage decision and it was not our intent to cover management of hypertension at that time. That hypertension was not covered in the earlier decision is supported by the fact that we have now been asked to make a specific coverage determination on TEB for this purpose. Because our intent in this regard may have been unclear in the original decision, any claims that were processed for this purpose under contractor discretion will not be re-examined.

The new evidence reviewed by CMS pertains only to patients with drug resistant hypertension. While the totality of the evidence is not sufficient to support a broad positive coverage determination for this use, it indicates that there may be situations in which TEB could be useful in monitoring of response to medication changes in treatment of drug resistant hypertension. Therefore,

- CMS determines that the coverage and description of the specifics of the situation in which TEB is reasonable and necessary for the treatment of drug resistant hypertension is left to carrier discretion.

Drug resistant hypertension is defined as failure to achieve goal BP in patients who are adhering to full doses of an appropriate three-drug regimen that includes a diuretic.

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  CMS also determines that the evidence is inadequate to conclude that TEB is reasonable and necessary for the management of all other forms of hypertension, and therefore its use for all other forms of hypertension is non-covered.

CMS found no evidence to support removing the noncoverage restrictions listed in the current national coverage policy. Therefore, TEB continues to be non-covered when used for monitoring of patients with:

- Proven or suspected disease involving severe regurgitation of the aorta;
- Minute ventilation (MV) sensor function pacemakers, since the device may adversely affect the functioning of that type of pacemaker; or
- During cardiac bypass surgery.

Due to an absence of evidence, all other uses of TEB not described in this memorandum are noncovered.

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Decision Memo

To: Administrative File CAG: 0001R
Cardiac Output Monitoring by Electrical Bioimpedance

From:

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Policy Analyst, CAG

Subject: Decision Memorandum for Electrical Bioimpedance for Cardiac Output Monitoring
Date: August 7, 2003

This memorandum serves four purposes: (1) provides a brief description of hemodynamic monitoring; (2) describes various methods of hemodynamic monitoring, with an emphasis on thoracic electrical bioimpedance (TEB); (3) presents and analyzes the available scientific and clinical literature on TEB for certain patient populations for the purpose of determining whether the current national coverage policy should be modified; and (4) announces our intent to refine the current national coverage policy for cardiac-related indications, to leave the decision regarding coverage of TEB for the management of drug resistant hypertension to contractor discretion, and to noncover TEB for all other indications.

I. Background

Hemodynamic monitoring generally refers to the measurement of parameters that pertain to the function of the heart and arterial system, such as pulmonary artery pressure and cardiac output. When performed invasively in patients with cardiac illnesses, this monitoring usually is reserved for hospitalized, seriously ill patients suffering from acute heart failure, acute myocardial infarction, primary pulmonary hypertension, or patients in need of perioperative monitoring for cardiac surgery. The data obtained from hemodynamic monitoring may help differentiate cardiogenic from noncardiogenic complications during treatment and guide both fluid and pharmaceutical management of these patients. Although hemodynamic monitoring by invasive means has been performed for nearly thirty years, questions about both its safety and utility have been raised recently.[1] A 1996 study by Connors et al. concluded that the procedure was associated with both increased mortality and use of resources.

Accurate assessment of fluid or volume status also may aid in the treatment of chronic cardiovascular disease in the outpatient setting. In ambulatory patients, this information is most often obtained by physical examination, which includes measurement of weight and blood pressure, auscultation of heart and lungs,[2] as well as assessment of venous jugular distension and peripheral edema. Invasive hemodynamic monitoring by means of insertion of an arterial catheter generally is neither necessary nor available in an outpatient setting. However, should a clinician wish to confirm findings from physical examination in complicated patients, or obtain more detail about the patient's volume status in order to better guide therapy, an accurate, noninvasive method of hemodynamic assessment could be useful.

Several studies claim that noninvasive hemodynamic measurements obtained by TEB correlate with invasive measurements and trend in the same direction. In the following section, we discuss the similarities and differences in data obtained by various methods of hemodynamic monitoring.

Methods of Hemodynamic Monitoring

Invasive Testing

Right heart catheterization (RHC) (also referred to as pulmonary artery catheterization) is both a diagnostic and a monitoring tool. Several different types of hemodynamic measurements can be made through cardiac catheterization, including right atrial pressure, right ventricular pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, cardiac output, and oxygen saturation. [3] The 1998 American College of Cardiology Expert Consensus Document (ACC Consensus Document), which discusses RHC, notes that it is useful for distinguishing between cardiogenic and noncardiogenic heart failure, monitoring hemodynamic compromise following an acute myocardial infarction, establishing the diagnosis of primary pulmonary hypertension, and monitoring patients perioperatively undergoing cardiac surgery.[4] The ACC Consensus Document notes that its recommendations are based primarily on published reports as well as expert opinion and that few data are available from well controlled clinical trials. Adverse events include arterial puncture, bleeding, nerve injury, inducement of arrhythmias, embolus and thrombus formation, and infection. The risk of the latter two significantly increases with catheters left in place for more than three to four days.

There are several variations in invasive RHC methodology, including direct and indirect Fick methods and various dilution methods.[5] The direct Fick method has been used frequently as a standard for comparison of hemodynamic data obtained by TEB.

Minimally Invasive Testing

Radionuclide angiography is a minimally invasive procedure used to assess hemodynamic parameters. The procedure involves small amounts of radioactive materials (tracers) that are injected into the patient’s body, which emit gamma rays that are detected by a sensing apparatus. Hemodynamic parameters are derived through dynamic sampling of left ventricular radioactive counts.

Non-invasive Testing

Echocardiography

Echocardiography uses ultrasound waves to produce recordings of the heart's anatomy and blood flow. Although this technique is used widely for the diagnosis of heart disease,[6] it is not usually used to obtain stroke volume and cardiac output because these particular measurement procedures are imprecise.[7] Echocardiography also may be performed invasively using a transesophogeal probe.

Thoracic Electrical Bioimpedance

TEB was developed in the mid-1960s for the National Aeronautics and Space Administration to monitor stroke volume and cardiac output non-invasively during space flight.[8] Since then, advances in computer technology have led to improvements in the quality of TEB. This procedure measures the total impedance, or resistance, to the flow of electricity in the thorax. Changes in this resistance are used to measure and calculate hemodynamic parameters.[9]

The primary hemodynamic measure obtained by TEB is stroke volume. Stroke volume is then used to calculate other measures, such as cardiac output, which is determined as the product of stroke volume and heart rate. TEB employs two pairs of electrodes placed at the neck and the chest to transmit and measure the thoracic impedance[10] of a high-frequency low-amplitude electrical current. Four electrodes are used-two at the base of the neck and two at the xiphoid-sternal junction. The difference between the amplitude of the voltage introduced into the thorax by the TEB device and the voltage sensed at the completion of the circuit is used to calculate stroke volume. Because blood is a good conductor of electricity, the change in voltage is a measure of impedance to flow and is inversely proportional to the amount of blood in the thoracic vasculature. Stroke volume is determined from the change in flow over a given period of time and measured during electrical systole using a software algorithm. Cardiac index (CI) is derived by dividing cardiac output by the patient's body surface area. A systemic vascular resistance index (SVRI) can be calculated from the CI and stroke volume. Thorax dimensions are part of the calculation algorithm, making proper placement of electrodes necessary to ensure accurate results.

The outer sensors emit a high frequency, low-amplitude electrical current that passes through the chest. The current flows through the aorta, which is the most conductive area because it is filled with blood. At this point, a baseline level of impedance is established. The changes in impedance that TEB measures are produced by variations in blood volume and velocity in the ascending aorta during systole and diastole. Thus, as the blood's velocity and volume in the aorta changes with each heartbeat, TEB measures changes in impedance to the electrical current. Thoracic impedance is calculated with each beat of the heart. During systole, the impedance decreases and during diastole, the impedance increases. The changes in impedance are a direct indication of aortic flow and, therefore, reflect left ventricular function.[11] By monitoring the changes in impedance to the electrical signal, TEB theoretically can provide continuous measures of stroke volume, which in turn can be used to calculate a continuous measure of cardiac output.[12] In addition to cardiac output and stroke volume, the following hemodynamic parameters can be determined through TEB: systemic vascular resistance; change in impedance over time; pre-ejection period; ventricular ejection time; acceleration contractility index; left cardiac work index; and thoracic fluid status.[13] TEB also provides serial measures of hemodynamic parameters, which can be used in trending.[14] Several factors have been identified that may limit bioimpedance for monitoring hemodynamic flow. For example, large amounts of fluid in the thorax, such as from pulmonary edema or pericardial effusions, may obstruct the impedance signal. In addition, arrhythmias may cause beat-to-beat variations in flow and valvular incompetence may affect the amount of forward blood flow, causing the hemodynamic measurements to be either unattainable or unreliable.

Typically, TEB measurements are performed by a single, properly trained person, such as a healthcare technician or nurse, during a visit with the treating physician. As a result, TEB does not require a separate visit and it is usually performed as an aid in patient management, similar to a pulse oximetry or review of laboratory tests, as a part of the treating physician's evaluation of the patient's condition. The TEB device generates values for several hemodynamic parameters that can be used by the physician, in conjunction with other data, to make patient management decisions. Since it is noninvasive, there are no complications associated with the test. The accuracy and clinical utility of TEB are the focus of this decision memorandum.

II. FDA Status

Companies manufacturing TEB devices have obtained clearance for marketing of these devices under the Food and Drug Administration's (FDA) 510(k) process.[15] The FDA considers TEB devices to be Class II devices.[16] The predicate devices upon which clearance was based are previous cardiac output monitors employing impedance plethysmography.[17] Several TEB devices have been cleared through the FDA for marketing to monitor hemodynamic parameters.

Although a device must receive FDA approval or clearance for at least one indication to be eligible for Medicare coverage (except for a category B device under an investigational device exemption clinical trial [60 FR 48417, September 19, 1995]), FDA approval/clearance alone does not entitle that device to coverage. To be covered by CMS, the device must fall under a Medicare benefit category and be considered reasonable and necessary for the diagnosis or treatment of an illness or injury or to improve the functioning of a malformed body member.

Regarding FDA 510(k) clearance, as we stated in 66 FR 58788-58797 (November 23, 2001), "[t]he criteria the FDA uses in making determinations related to substantial equivalency under section 510(k) of the Food, Drug, and Cosmetic Act is significantly different from the scientific evidence we consider in making ‘reasonable and necessary’ determinations under Medicare. The FDA does not necessarily require clinical data or outcomes studies in making a determination of substantial equivalency for the purpose of device approval under section 510(k) of the Food, Drug, and Cosmetic Act. Medicare evidence-based national coverage determinations consider medical benefit and clinical utility of an item or service in determining whether the item or service is considered reasonable and necessary under the Medicare program. Thus, a substantial equivalency approval under section 510(k) of the Food, Drug, and Cosmetic Act is not sufficient for making a determination concerning Medicare coverage.”

III. History of Medicare’s Coverage on TEB and Timeline of Recent Activities

History of Medicare Coverage of TEB

On September 22, 1998, CMS issued a positive national coverage determination for TEB, for six indications. The policy became effective on July 1, 1999 (Coverage Issues Manual §50-54). Prior to this decision, TEB was non-covered. The six covered indications are:

- Noninvasive diagnosis or monitoring of hemodynamics in patients with suspected or known cardiovascular disease;
- Differentiation of cardiogenic from pulmonary causes of acute dyspnea;
- Optimization of atrioventricular interval for patients with A/V sequential cardiac pacemakers;
- Patients with need of determination for intravenous inotropic therapy;
- Post-heart transplant myocardial biopsy patients; and
- Patients with a need for fluid management.

The national coverage policy also states that “[n]ot covered at this time are the use of such devices for any monitoring of patients with proven or suspected disease involving severe regurgitation of the aorta, or for patients with minute ventilation (MV) sensor function pacemakers, since the device may adversely affect the functioning of that type of pacemaker. Also, these devices do not render accurate measurements in cardiac bypass patients while on a cardiopulmonary bypass machine, but do provide accurate measurements prior to and post bypass pump.”

Timeline of Recent Activities

In December 2001, Dr. Laurence Clark, Carrier Medical Director (CMD) for Trailblazer Health Enterprises requested that CMS reconsider the policy issued in 1999 due to concerns regarding the accuracy, consistency, and verifiability of the data derived from TEB, in addition to questions regarding the usefulness of the device. Dr. Clark asked that CMS reconsider its policy on TEB for all six indications covered under the policy and in addition to consider a seventh, new indication, which is the management of hypertension.

An outline of events surrounding the national coverage determination review follows:

December 6, 2001	CMS accepted the request from Dr. Laurence Clark, CMD for Trailblazer Health Enterprises, for a reconsideration of the national coverage determination on TEB. He requested that CMS reevaluate the scope of the existing policy and to consider adding the management of hypertension.
February 4, 2002	CMS formally commissioned a technology assessment (TA) from the Agency for Health Research and Quality (AHRQ) due to the large volume of relevant clinical studies and the complexity of the scientific issues. AHRQ ultimately selected the New England Medical Center (NEMC) as the evidence-based practice center for the TA.
February 19, 2002	CMS met with representatives from CardioDynamics, Inc., at their request, to discuss issues surrounding the request for reconsideration. CardioDynamics manufacturers BioZ, a type of TEB device. The company was the requestor for the 1999 national coverage determination.
April 25, 2002	CMS again met with representatives from CardioDynamics, Inc., at their request, to discuss further issues surrounding the request for reconsideration.
May 3, 2002	CMS posted the final TA questions on its web site.

November 7, 2002	CMS again met with a representative from CardioDynamics, Inc., at the company's request, to discuss issues surrounding the request for reconsideration.
November 29, 2002	CMS received the final TA from AHRQ.
December 13, 2002	CMS again met with representatives from CardioDynamics, Inc., at the company's request, to discuss issues surrounding the request for reconsideration.
April 2, 2003	CMS met with Congressman Cunningham to discuss issues surrounding the request for reconsideration.
May 9, 2003	CMS met with a representative of CardioDynamics, Inc., and a physician for a demonstration of the BioZ device.

IV. General Principles for the Evaluation of Diagnostic Tests

When CMS reviews a diagnostic test for a national coverage determination, among other things, it evaluates whether the test is reasonable and necessary. CMS considers the test performance of the diagnostic and its impact on patient management (42 C.F.R. § 410.32), i.e., does its use lead to improved net health outcomes in the Medicare population?

An important consideration in reviewing whether a diagnostic test is reasonable and necessary is its validity (sensitivity and specificity) and reliability (inter-observer reliability) when compared to an existing diagnostic test (best available reference test, preferably a "gold standard") used for the same purpose. Sensitivity refers to the ability of a test to identify correctly patients who have the disease as identified by the reference test. Specificity refers to the ability of a test to identify correctly patients who do not have the disease. Diagnostic test validity also depends on when, in the course of disease management, the test is conducted. The diagnostic test should be able to provide information that is at least as accurate or complementary to the best available reference test. Although in the absence of a gold standard, it may not be possible to determine the value of a test without the availability of clinical studies demonstrating that its use improves net health outcomes at least as well as the best available reference test. However, even if the information provided by the test is accurate and does not alter patient management, CMS may determine the test is not reasonable and necessary for a given condition.

When reviewing studies that investigate a diagnostic modality, important aspects of the study design include, but are not limited to, the following:

1. The study uses a credible reference standard;

2. The reference standard is interpreted independently from the diagnostic test of interest, and the observers have no knowledge of the results of the other test;

3. Patients are selected with as little bias as possible;

4. When possible, an analysis of inter-observer reliability is conducted for both the reference and the diagnostic test under consideration; and

5. The analysis addresses variables that may affect test results.

V. Summary of Evidence

CMS performed an extensive literature review in order to address the following analytic questions:

- What is the accuracy of TEB relative to other tests of hemodynamic parameters?

- What is the clinical utility of TEB for the six indications covered in the existing coverage policy?
- What is the clinical utility of TEB in the management of hypertension?

As part of this review, CMS took into consideration an existing TA, an updated TA contracted for the purposes of this review, submissions from a manufacturer of TEB devices, published clinical studies, clinical guidelines from professional societies, and public comments. We continued to search for new clinical studies through mid-February 2003.

Evidence for Accuracy of TEB Measurements

With respect to the issue of accuracy, it is necessary to describe how numeric data are presented in the TEB literature. The majority of published scientific material relating to TEB describes it in relation to another method of hemodynamic monitoring, most often to thermodilution. The relationship between the two measurement techniques is then expressed in the form of a correlation coefficient demonstrating that the two techniques produce similar results. While correlation coefficients can compare results of one diagnostic test to another, they cannot show the accuracy or clinical utility of either test. The 2002 TA that CMS commissioned for purposes of this review (see below) stated that correlation coefficients were poor summary indicators of the relative performance of these diagnostic tests because of "the dependence of the correlation on the distribution of true cardiac output levels in the study sample [and] the fact that even when the correlation coefficient is close to one, there can be large systematic differences or random variations in individual measurements." The TA noted that the reported correlation coefficients found in reviewing the available literature ranged from –0.01 to 0.97. In specific examples, they noted a correlation coefficient as high as 0.879 in comparing three similar studies,[18] but with a wide confidence interval (0.642-0.962), which limited the inferences that could be drawn from the comparison. In another example of the variability of reported results, a group of three other studies had a correlation of 0.349 with a confidence interval of 0.122-0.541.

The 2002 TA that CMS commissioned also suggested that bias and limits of agreement[19] as described by Critchley and Critchley (1999) and Bland and Altman (1986) were better measures of the performance of diagnostic tests than were correlation coefficients. However, the TA also noted that bias rarely was reported in the TEB literature. When bias was reported, it sometimes was based on inappropriate measures. As a specific example, the TA stated that the three studies "with the largest bias in cardiac output…shared a common characteristic" in that they failed to control for the variability in thermodilution measurements.

Both the TA and the CMS assessments of the accuracy of TEB measurements are limited by the presentation of data in the available literature as noted in the two proceeding paragraphs.

Technology Assessments

Agency for Health Care Policy and Research (1992)

The Agency for Health Care Policy and Research (AHCPR)[20] published an assessment entitled “Measuring Cardiac Output by Electrical Bioimpedance” in September 1992. The goals of the assessment were to determine “whether the measurement of cardiac output (CO) by bioimpedance is accurate, safe, clinically useful, and equivalent to thermodilution techniques” and to address “the appropriateness of bioimpedance measurements of CO on an outpatient basis.” At the time of that assessment, it was found that “there are no published data that relate CO measurements by EB [electrical bioimpedance, which is referred to as thoracic electrical bioimpedance in this decision memorandum] to patient outcomes. Virtually all studies of EB report comparative results of EB measurements of CO with those obtained by other methods.” The assessment also found that “results of these comparisons were commonly reported as correlation coefficients (*r*), with subsequent conclusions by the investigators that EB provided satisfactory estimates of CO if correlations were approximately in the range of .80-.90 and that EB did not provide reliable estimates of CO if *r* was less than .70.” However, the rationale for selecting these levels of correlation was not made explicit.

The AHCPR assessment noted the following: “the precision and accuracy of EB is significantly reduced in patients with cardiac valve lesions and in the presence of intracardiac shunts, pacemakers, sepsis, mechanical ventilation, dysrhythmias, or other conditions associated with extremely high or low levels of CO” and that “…other factors that may potentially affect the accuracy of EB include fluid in the lungs or pleural space, assisted ventilation, the nonuniform changing volume of blood along the length of the thorax, changes in blood resistivity, movement artifacts, electrode type and placement, and the method used to determine signal sampling.”

In the period since the publication of the AHCPR assessment, there have been advances in equipment and computer technology that have improved the technical quality of data obtained by TEB. However, much of the earlier criticism of the scientific data presented to support the utility of the measurement of cardiac output by bioimpedance remains valid. For example, the AHCPR assessment notes: "the general clinical utility of (CO) measurements in many types of ill patients has been questioned, and controlled clinical trials establishing improved patient outcome from their use have not been performed." Since the publication of the AHCPR assessment, few such studies have been performed. The studies that have been completed since 1992 are largely comparisons between TEB and other methods of hemodynamic monitoring, which document the similarity of trending obtained by each of the methods studied. How the data obtained from TEB testing is used to change the clinical course of a patient's treatment and how a patient's condition benefits from that data has not, for the most part, been explored.

The AHCPR assessment also notes that "criteria for the appropriate selection of subsets of patients for whom EB determinations of CO may be most useful have not been delineated or validated." Further, the report concluded that "no published studies have specifically addressed the use of EB in the outpatient setting, and its potential use in this context remains conjectural."

Agency for Healthcare Research and Quality (2002)

CMS contracted with AHRQ for the performance of a new technology assessment of TEB that would cover scientific literature published subsequent to the AHCPR assessment, with a particular emphasis on the following: the utility of TEB in the treatment of the indications already covered by Medicare, its utility in the management of hypertension, and any improvements in the technology of the equipment. Furthermore, the request specified our interest in studies that looked at patient outcomes based on TEB. The TA was performed by New England Medical Center (NEMC). Our summary of its principal findings is provided below.

The 2002 TA conducted a systematic review and meta-analysis of the TEB literature. NEMC searched MEDLINE for the period from 1966 through January 2002 using synonyms for “impedance cardiography.” The search strategy was restricted to the English language and to human subjects. This search yielded more than 8000 articles. An updated search was performed on July 22, 2002. The criteria for review of articles included a publication date of 1991 or later, discussion of the methodology of TEB as a diagnostic and/or monitoring tool, or analysis of TEB in comparison to another diagnostic technique for the clinical indications of interest. Approximately 275 articles were reviewed, 78 of which were included in the evidence tables of this report. (The 2002 TA assessment also reviewed a number of abstracts related to TEB. Abstracts have not been included in the CMS assessment of the TEB literature, as they do not provide sufficient detail on which to make sound judgments regarding their scientific validity.)

The 2002 TA addressed the following issues.

1. A review of the diagnostic test performance of TEB for hemodynamic measurements, specifically: cardiac output, stroke volume, contractility, systemic vascular resistance, and thoracic fluid, including the following elements:
    - Comparison of the diagnostic test performance of TEB to alternative tests.
    - A review of information from clinical literature (if any) on any factors that may affect the test performance of TEB (for example, placement of leads, experience of the operator, comorbid conditions) and the limitations that these factors would place on the clinical utility of TEB.
2. A review of the clinical literature on the utility of TEB for the following seven indications, with a focus on data demonstrating changes in patient management and/or improved health outcomes resulting from the device:
    - Noninvasive diagnosis or monitoring of hemodynamics in patients with suspected or known cardiovascular disease,
    - Differentiation of cardiogenic from pulmonary causes of acute dyspnea
    - Optimization of atrioventricular interval for patients with A/V sequential cardiac pacemakers,
    - Patients with need of determination of intravenous inotropic therapy
    - Post heart transplant myocardial biopsy patients,
    - Cardiac patients with a need for fluid management, and
    - Management of hypertension.
3. A review of the setting of the clinical studies of bioimpedance (inpatient vs. outpatient vs. emergency department) and issues related to the applicability of data from the inpatient to other settings.
4. A review of any information available in the clinical studies of the conditions specified in Question 2 regarding the training of persons using the devices and any issues related to this training (e.g., must monitoring data be interpreted only by a cardiologist, does the administration of the test require special training, and can it be performed by a non-physician?).

Most of the studies reviewed in this TA were similar to those reviewed in the 1992 AHCPR assessment, in that measures of cardiac output and other hemodynamic parameters by TEB were compared for accuracy and trending with other methods of measuring such parameters (both invasive and non-invasive). Most frequently, these studies reported findings in seriously or critically ill inpatients, with no indication that data from TEB were used to make treatment decisions. Recent studies by Shoemaker et al.[21] and others on the use of TEB in the emergency room to identify patients likely to need early intensive monitoring also did not evaluate how TEB impacts patient management or health outcomes.

The following is a summary of the 2002 TA findings:

Known or Suspected Cardiovascular Disease

The 2002 TA states: "No studies provided information on health outcomes or patient management or on clinical end-points to address the usefulness of TEB in monitoring or management." Among the studies reviewed, a 2000 study by Greenberg et al. reported small changes in hemodynamic measurements in stable heart failure patients after brief hall walks and the reproducibility of those changes one week later. The purpose of the study, however, was to show that changes did occur with moderate exercise and that the data could be reproduced over a short period, not to show how this information could be used in the better treatment of heart failure. The authors of the Greenberg et al. study stated: "The central limitation of this study lies in incomplete data for the short and long term outcomes for this group of patients and the lack of serial measurements over time."

We mention the studies specifically cited in the TA only briefly, as they did not provide clinical outcomes information directly related to diagnosis or management of patients with cardiovascular disease:

1. 1993 study by Kasznicki and Drzewoski comparing the effects of chemotherapy on hemodynamic measures not related to cardiovascular disease;
2. 1997 study by Scherhag et al. of the hemodynamic effects of various pharmacological agents used in stress testing in patients with suspected coronary artery disease. The study included no validation of the variation in test results to confirm a relationship to cardiovascular disease;
3. 1998 study by Raaijmakers et al. showing relatively poor correlation between TEB and invasive measures of lung water volume in ICU patients with acute respiratory failure not resulting from cardiovascular disease;
4. 1999 study by Zerahn et al. on improved lung function following thoracocentesis in patients with pleural effusion due to malignancy or heart failure. Improved lung function, rather than improved cardiovascular function, was the focus of the study; and
5. 2000 study by Tatevossian et al. using TEB to monitor the development of acute respiratory distress syndrome (ARDS).[22]

Differentiation of Cardiogenic from Pulmonary Causes of Acute Dyspnea

The 2002 TA literature search did not identify any studies that evaluated the accuracy of TEB in distinguishing cardiogenic from pulmonary causes of acute dyspnea. Also, the TA states: "No studies…were found that evaluated the clinical impact on patient management and/or improved health outcomes from the use of TEB monitoring for differentiation of cardiogenic from pulmonary causes of acute dyspnea." Several abstracts, which potentially might have provided information relating to this indication, were identified in the NEMC literature search, but none resulted in a complete, peer reviewed published study available for analysis.

Optimization of Atrioventricular Interval with A/V Sequential Pacemakers

A number of studies in the early 1990's proposed that TEB measurement of cardiac output could be utilized in determining an optimal A/V delay when programming a pacemaker. The 2002 TA located three more recent studies relating to this use of TEB:

1. 1997 study by Kindermann et al. comparing A/V delay determined by TEB to that derived using pulsed Doppler echocardiography. The study did not look at health outcomes that might be attributable to either method. The purpose of the study was to validate Doppler measurement against TEB, but not to offer TEB as a substitute for Doppler;

2. 1998 study by Haennel et al. where TEB was used to monitor the effects of exercise testing in pacemaker dependent patients. There was no attempt to use TEB to change pacemaker settings. Rather, it was used to assess the patient's response to an exercise protocol. TEB was not used to guide patient management;
3. 1999 article by Belott et al. supporting TEB for pacemaker optimization that did not include any clinical data in support of its observations and recommendations.

The 2002 TA concluded: "Some of the …evidence suggests that TEB is potentially useful in patients with pacemakers…. None of the studies reported health outcomes after adjustment of the A/V delay, so the evidence is insufficient to conclude whether TEB optimization of the A/V delay improves health outcomes." The studies also do not establish that changes made based on cardiac output data from TEB lead to an optimization of A/V interval.

Determination of the Need for Intravenous Inotropic Therapy

The 2002 TA literature search did not identify any studies that evaluated the clinical impact on patient management and/or improved health outcomes that would support this use of TEB.

Post-Heart Transplant Myocardial Biopsy

The 2002 TA literature search identified a 1993 study[23] suggesting that TEB potentially might supplement biopsy as an early indication of rejection of a transplanted heart. While the TA concluded that the preliminary findings from that study might be useful if replicated, NEMC was unable to locate any subsequent, complete, published peer-reviewed studies relating to TEB for post-heart transplant myocardial biopsy.

Patients in Need of Fluid Management

The 2002 TA literature search did not identify any complete, published peer-reviewed studies containing information regarding clinical outcomes related to TEB for fluid management. Studies relating to whole body impedance, which has been used for assessing fluid status, were not included in the assessment, as they relate to a technology that is different from TEB.

Management of Hypertension

One study (Taler et al., 2002)[24] reported patient outcomes related to TEB for management of hypertension. This study was a randomized, prospective trial of TEB compared to specialist care in guiding drug selection for patients with resistant hypertension. In this study, patients who were monitored with TEB had a "small, but statistically significant greater decrease in blood pressure compared to patients treated using clinical judgment….". The study began with a 4 mm Hg systolic blood pressure and a 4 mm Hg diastolic blood pressure difference between the specialist care group and the hemodynamic monitoring group and ended with an 8 mm Hg difference in systolic blood pressure and a 7 mm Hg difference in diastolic blood pressure. The TA noted weaknesses in the study related to randomization and blinding. NEMC also noted "significantly more frequent changes in medications and dosages were made in the hemodynamic group as compared to the specialist care group….". Further, "[t]he authors commented that the specialist care group was comprised of nationally certified hypertension specialists with special expertise in the treatment of resistant hypertension, and suggested that monitoring with TEB would have a greater benefit when the alternative was management with a community physician…. It is, therefore, not known what the benefit of TEB would be in community practice with treatment decisions made by generalists." In addition, the TA acknowledged that "it is also possible that the small improvement in the hemodynamic monitoring group was due not only to the use of TEB, but to correct application by the treating physician of the algorithm in the authors' Table 1 that guided the use of TEB in this application. Before it could be known what the benefit of TEB would be in community practice, with treatment decisions made by generalists, the ability of generalists to learn and apply this algorithm in conjunction with TEB would need to be demonstrated and evaluated."

NEMC pointed out in its conclusions that the Taler study "is an example of the type of study that needs to be done; it evaluated the use of TEB in managing patients with resistant hypertension and examined hypertension, an important outcome, that is a well-accepted surrogate for other important outcomes. The…study demonstrates the importance of a control group…patients in the TEB and control group both experienced large reductions in blood pressure; therefore the majority of the effect in the study is attributed to other factors that are common to both the control group and the intervention group such as access to the expert specialists. The results may not be generalizable in a community setting."

Year of Publication and Manufacturers

To evaluate whether or not newer technologies are more accurate than earlier versions, the 2002 TA compared correlation coefficients reported in the literature during 1991-1996 and during 1997-2002. The combined correlations coefficients were 0.756 (95% CI: 0.639-0.838) and 0.487 (95% CI: 0.299-0.640) respectively. Most of the studies used devices that are no longer manufactured. Accordingly, there was insufficient data available on currently marketed machines for the TA to draw conclusions.

Other Issues

There was inadequate data for the 2002 TA to draw conclusions about factors that may affect test performance, training requirements for TEB, or use in outpatient and emergency room settings.

Summary

The 2002 TA summarizes its findings as follows: "Due to limitations in the studies, no meaningful conclusions can be drawn about the accuracy of TEB, compared to alternative measures of hemodynamic parameters. There is also little conclusive evidence regarding TEB's usefulness in the specific clinical areas addressed…. Despite the large amount of observational data generated on TEB, almost all of the studies did not use a design that would allow for meaningful comparisons of patient outcomes of care and thus would provide evidence to address the questions (posed by CMS). In several of these reports the authors anecdotally stated in their discussion section that they found the method to be clinically useful and helpful for managing patients under various critical circumstances (or the opposite); however, these inferences were not based on randomized or comparative designs where a group of patients was monitored by TEB and contrasted with a control group." Also, "[t]he clinical reports on the use of TEB for a variety of clinical indications…published since 1991 suggested that this non-invasive method is of interest and may potentially support some of these indications, but there is little evidence that directly addressed how this monitoring technique can affect patient outcomes…. There was little conclusive evidence regarding TEB's usefulness in the specific areas addressed, and this was largely due to the lack of focus of researchers in this area on clinical outcomes."

Articles Reviewed by CMS

CMS staff reviewed the studies that NEMC included as part of their TA. A manufacturer of TEB devices requested that we give special attention to two articles (Sageman et al., 2002, and Taler et al., 2002), both of which were included in the 2002 NEMC TA, as well as all articles pertaining to its product. This manufacturer highlighted the article by Taler et al. because it was the only available study that provided clinical outcomes data for TEB in the management of resistant hypertension. The manufacturer also emphasized the article by Sageman et al. because the manufacturer considered it to demonstrate the accuracy of TEB when compared with invasive monitoring. The manufacturer also submitted additional articles and abstracts, which we have reviewed. However, as indicated above, we generally give little weight to abstracts, because they do not include sufficient study details or data upon which we can make a sound judgment of study validity. In addition, we did not include articles that were editorial in nature or those that were not supported by clinical data on TEB. Because of the interest of one of the TEB device manufacturers in our review of the Sageman and Taler articles, we provide a detailed analysis of them below.

The purpose to the article by Sageman et al., published in February 2002, was to compare TEB to another method of hemodynamic measurement (in this case pulmonary artery thermodilution [TD]). Twenty post-coronary bypass or valve replacement patients were monitored by both methods during their first 12 to 18 hours in the ICU. There is no information provided about the method of patient selection or clinical characteristics of study patients, nor is there any discussion of what impact, if any, there may have been on the study results from combining patients with two different types of heart surgery.

The researchers sought to show that there was agreement in cardiac index values between TEB and TD when simultaneously measured throughout the monitoring period of up to 18 hours. Data for some patients had as few as four TEB measurements, while others had as many as 25 measurements during the study period, with data recorded “whenever the clinical situation warranted”. There is no description of the factors that triggered a measurement. The large differences in the numbers of observations for each patient introduced a significant potential for bias into the study, with some patients over-represented and others under-represented.

The authors state: “In most cases, exact numbers for cardiac index are not necessary for clinicians to feel comfortable: ranges and trends or movements in the data are what drive decision making.” The authors reasoned that small differences in the actual measures by each method could be accepted by clinicians “as long as both measures showed the same degree of relative movement over time.” The data presented are paired snapshots of patient hemodynamics recorded at irregular time intervals, and it is not possible to determine whether TEB and TD followed the same trend during the entire monitoring period. The study does not connect individual readings over time for each patient and then compare the results from the two measurement techniques. As a result, it cannot be determined if both devices provided similar estimates of the cardiac index over time nor if there were any differences between TEB and TD in terms of the magnitude and direction of hemodynamic changes. If there were such differences, it cannot be concluded that they were sufficient to affect the clinical management of a patient.

In all, 216 paired readings were obtained for the 20 patients. The data were arrayed and displayed graphically by several methods. Although the plot in Figure 1 of the article appears linear, only 95 readings are visible. If the remaining values are under other readings, an alternative presentation of the readings would have been more helpful. The data also demonstrates a wide cardiac index range. Typically, methods tend to differ most at the extremes and least in the middle range. In this study, the opposite is true.

The authors offered the following summary of their study: “…TEB and TD cardiac index in 20 patients after CPB [cardiopulmonary bypass] are linearly related, quantitatively equivalent in mean and variance, and highly concordant across patients and track well over time. TEB and TD follow the same pattern of increase and decrease *most* of the time and are matched perfectly >50% of the time. TEB in the ICU after CPB is a promising noninvasive, potentially low-cost alternative to TD and PAC (pulmonary artery catheterization) hemodynamic measurement. Much work remains to prove time-tested clinical utility and patient outcome improvement by using TEB. The authors believe that this technology shows a great deal of promise.”

The Taler et al. (2002) study provided the best evaluation of this technology for the management of a specified disease state (drug resistant hypertension). Patients were selected to participate in the study from among those patients who had been referred to a specialty hypertension clinic for failing to achieve a blood pressure of <140/90 mm Hg while taking $\geq$ 2 antihypertensive agents in apparently adequate doses. At the clinic, the patients were evaluated by a certified hypertension specialist, who screened them for secondary causes of hypertension and noncompliance with previously recommended therapy that would prevent achievement of blood pressure control. In a thirty-one month period, 117 of these patients were invited to participate in a three-month intensive treatment program.

Patients participating in the study were assigned randomly to treatment based on serial hemodynamic measurements (by TEB) and a predefined algorithm of medication changes used by one hypertension specialist (the lead investigator), or to treatment guided by a hypertension specialist without either TEB or a predefined treatment plan. Patients could be seen by one of several specialists, but the exact number of specialists who participated in the study was not reported.

Hemodynamic measurements were obtained for participants in both arms of the study upon entry. However, the data was stored for the specialist care group and the hemodynamic measurements were not repeated for these patients until the end of the study. All patients in both arms of the study were seen for blood pressure measurements “at least” monthly. A listing of patient data shows that patients in both arms of the study were seen by the nurse taking blood pressure measurements a mean of 6.2 times during the 90-day study period or roughly every two weeks. Patients in the hemodynamic-guided treatment arm also received monthly TEB measurements. CMS contacted the author for additional information about visit frequencies and was advised that some patients had as few as four visits during the study, but others, who were undergoing medication changes, were seen more frequently. The TEB group received more changes in medications and dosages. According to the lead investigator, TEB measurements were made during nurse visits for those in the TEB arm and did not require separate visits.

Medications for patients in the hemodynamic-guided treatment group were chosen according to the drug algorithm, but details of the treatment algorithm for medication use (e.g., dosages) for patients in the TEB arm are not presented. Also, the article does not provide values for the cardiac index, systemic vascular resistance index, or change in thoracic fluid impedance upon which treatment decisions would be (and were) based. For each of three potential hemodynamic profiles suggested by TEB data, several classes of drugs were available for use requiring clinical judgment by the practitioner in choosing specific medications and doses (see below). Using the treatment algorithm in addition to TEB introduced a second variable into the experimental group, as opposed to the specialist treatment group that used neither. The treatment algorithm is reproduced below:

Hemodynamic Care Algorithm

CI	SVRI	Medication Choices
Low	High	1. Add or increase dihydropyridine calcium channel blocker, ACE inhibitor, angiotensin receptor blocker, or direct vasodilator. 2. Reduce ß-blocker. 3. Evaluate D thoracic fluid impedance; if reduced, add or intensify diuretic dose.
High	Low	1. Add b-blocker or central agonist. 2. Reduce vasodilators. 3. Evaluate D thoracic fluid impedance; if reduced, add or intensify diuretic dose.
Normal	Normal	Evaluate D thoracic fluid impedance; if reduced, add or intensify diuretic dose.

The authors summarized the care of the hemodynamic-guided group as follows: "…if cardiac output was less than normal and/or systemic vascular resistance higher than normal, an agent with vasodilatory properties was added or the dosage was increased. Agents that reduce cardiac output were reduced in dosage or discontinued. Alternatively, if cardiac output was above normal and/or systemic vascular resistance was below normal, a b-blocker [beta blocker] or central sympathetic agonist[25] was added or increased in dosage, or vasodilatory agents were reduced in dosage or withdrawn. In all cases, attention was addressed to impedance change with posture…. Reduced change in impedance with posture (<3 ohms) in association with an elevated blood pressure was interpreted to suggest excess cardiopulmonary volume. In such instances, the diuretic dosage was increased, a more potent diuretic was prescribed, or a second diuretic was started."

Thirteen patients were excluded from the study for various reasons, leaving data on 104 patients for analysis. At the end of the study, mean systolic blood pressure in the hemodynamic-guided treatment group was reduced from 169 to 139 ± 2 and in the specialist care group from 173 to 147 ± 2 and the mean diastolic blood pressure was reduced from 87 to 72 ± 1 and from 91 to 79 ± 1 for each group, respectively. Although patients enrolled in this study had "resistant hypertension," both groups experienced large reductions in blood pressure in this short-term study, whether or not TEB was used. The difference in reduction in blood pressure between the groups, however, was statistically significant ($p<0.01$). The hemodynamic-guided group, which began the study with a mean systolic blood pressure 4 mm Hg lower than the specialist care group, achieved a 30 mm Hg decrease compared to a 26 mm Hg decrease for the specialist care group. The hemodynamic-guided group also began the study with a mean diastolic pressure of 87 and achieved a 15 mm Hg decrease compared to the specialist care group, which began with a mean diastolic pressure of 91 and achieved a 12 mm Hg decrease. Twenty-eight of 50 (56%) patients in the hemodynamic-guided group and 18 of 54 (33%) patients in the specialist care group achieved blood pressures of ≤ 140/90 ($p<0.05$).

Medication changes were frequent for patients in both arms of the study with the hemodynamic group undergoing 5.8 ± 0.4 changes and the specialist group undergoing 4.6 ± 0.5 changes. The most significant change was a near doubling of diuretic dosing in the hemodynamic group from 1.1 ± 0.1 doses per day to 2.1 ± 0.2 doses per day using dosage equivalents developed by the World Health Organization. This is in contrast to diuretic doses in the specialist group that virtually were unchanged going from 1.2 ± 0.2 to 1.4 ± 0.1.

The authors state that "(m)ean cardiac index did not change during the trial for either group. At entry, systemic vascular resistance was elevated above normal levels in both groups. Intensive drug treatment reduced systemic vascular resistance, with greater incremental reduction in the hemodynamic group." The article includes graphs to support these findings, but actual numbers for the cardiac index and systemic vascular resistance index are not reported in the study.

The authors state that "targeted control of volume using diuretic therapy achieved blood pressure control superior to that attained by empiric selection of drugs." As evidence that a change in fluid volume was responsible for the change in blood pressure in study participants, volume indicators obtained by TEB measurement are presented. Thoracic fluid impedance measured in ohms was recorded for all participants, both supine and standing, upon entrance into the study and at its conclusion. The mean supine measurement for the hemodynamic group was @1 ohm lower upon entry and their change with positional change is @ 1 ohm higher than the specialist care group. At the completion of the study, thoracic fluid impedance had increased @ 2.5 ohms in the hemodynamic group and @ 2 ohms in the specialist group, with a difference between groups with positional change of 0.7 ohms. While the authors state that "low absolute impedance values and diminished impedance change with posture at entry indicated expanded cardiopulmonary volume in our patients," the authors do not indicate what a normal fluid volume would be, or how many patients were able to achieve it. The authors do state that "[i]mpedance levels rose with more intensive diuretic dosage in both treatment groups suggesting a reduction in cardiopulmonary volume, although we did not see an incremental rise with the higher doses used in the hemodynamic group."

The authors further state that “improved blood pressure control…correlated with an incremental reduction in systemic vascular resistance in those treated according to hemodynamic values,” but include those values in graph format only without the actual numbers. While the article states that “(b)etter blood pressure control rates did not correlate with greater total numbers of medications,…or any particular drug class,” it also acknowledges that “(t)here were…more changes in medication choices and treatment intensity in the hemodynamic care group.”

Differences Between Devices

Additionally, CMS was asked by a manufacturer of TEB devices, CardioDynamics, Inc., to review a prepublication article evaluating 53 patients who were post-coronary artery bypass graft, that demonstrated superior accuracy of its device. Neither that article nor any other found in the CMS or the 2002 TA’s literature searches reported a head-to-head comparison between two manufacturers’ devices.

CMS also evaluated the literature pertaining to CardioDynamics’ BioZ device on its own merits. The majority of studies exist only in abstract form and subsequently have not been published as complete, peer reviewed studies. With the exception of the Taler et al. article, none of the studies assesses the impact of BioZ on patient management. One prepublication article pertaining to patients in the emergency room that suggests that TEB may be useful to distinguish cardiogenic from pulmonary causes of acute dyspnea, contains important flaws that make it difficult to draw any firm conclusions.[26] The remainder of the published studies did not compare CardioDynamics’ device to other tests of hemodynamic parameters; were case series describing how TEB was used in patients without systematic evaluations of the impact of TEB on patient management; or compared the device to other tests of hemodynamic parameters, such as TD. Notably, Drazner et al. (2002) found that the “upper and lower levels of agreement between the thermodilution and impedance cardiac indexes suggest that these two measurements will usually be within $\pm$ 1.2 L/min/m^2 of each other.” From a clinical practice standpoint, a cardiac output reading that is off by 1.2 L/min/m^2 can be significant and could impact treatment decisions adversely.

CMS and NEMC identified two clinical guidelines from professional societies that were relevant to our coverage review of TEB. Pertinent information from these guidelines is highlighted below.

American College of Cardiology/American Heart Association 2001 Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult[27]

With reference to the common need to assess fluid or volume status in heart failure (HF) patients, these guidelines state: "The physical examination is the primary step in evaluating the presence and severity of fluid retention in patients with HF…the role of periodic invasive or noninvasive hemodynamic measurements in the management of HF remains uncertain…. Although hemodynamic measurements can…be performed by noninvasive methods such as transthoracic bioimpedance, routine use of this technology cannot be recommended at the present time because the accuracy of bioelectrical parameters has not been defined in patients with chronic HF and it has not been shown to be more valuable than routine tests, including the physical examination. Moreover, it is not clear whether serial noninvasive hemodynamic measurements can be used to gauge the efficacy of treatment or to identify patients most likely to deteriorate symptomatically during long-term follow-up."

Although these guidelines were examined primarily to determine if they contained recommendations about the use of noninvasive hemodynamic measurements in the outpatient care of heart failure patients, CMS noted that they also contained material on the use of inotropes in the outpatient setting. This raised serious concerns about such use except for the need for continuous infusions in the care of terminal heart failure in a patient choosing to die with comfort at home or in patients awaiting cardiac transplantation at home. The guidelines state: "Because of lack of evidence to support their efficacy and concerns about their toxicity, physicians should not utilize *intermittent* infusions of positive inotropic agents (at home, in an outpatient clinic, or in a short-stay unit) in the long-term treatment of HF, even in its advanced stages…. However, *continuous* inotropic support can provide palliation of symptoms as part of an overall plan to allow the patient to die with comfort at home. The use of *continuous* intravenous inotropic support to allow hospital discharge should be distinguished from the *intermittent* administration of infusions of positive inotropic agents to patients who have been successfully weaned from inotropic support. The long-term use of regularly scheduled *intermittent* infusions at home, in an outpatient clinic, or in a short-stay unit is strongly discouraged, even in advanced HF."

ACC/AHA/NASPE 1998 Practice Guidelines for Implantation of Cardiac Pacemakers and Antiarryhthmia Devices[28]

A search of these clinical guidelines failed to find any reference to the current use of TEB in pacemaker programming.

CMS did not find any major clinical guidelines, including hypertension guidelines, from a professional society or appropriate government body, such as the Veterans Administration or the National Institutes of Health that recommend the use of TEB for diagnosis, monitoring or treatment of any illness or injury.

Public Comments

CMS received 34 letters in support of TEB. Twenty-six letters were received from physicians, including nine from members of the Medical Advisory Board of CardioDynamics, a manufacturer of TEB devices. Five letters were received from Medicare beneficiaries, two from members of Congress, and one from the Rainbow Coalition. Nine letters expressed the authors' positive experiences with TEB in addition to voicing concern about the possibility of Medicare withdrawing coverage of TEB. Two letters, both of which were submitted by physicians, did not mention Medicare coverage of TEB, but rather expressed the writers' positive experiences with the device, emphasizing that it has clinical utility. Eighteen of these letters were sent by individual physicians in response to the posting of the 2002 TA on our coverage website. These letters made the following general comments: 1) TEB is a useful technology for the indications currently covered as well as for managing hypertension; 2) the 2002 TA was too negative about TEB; 3) the 2002 TA erred by considering studies involving devices no longer marketed today and not focusing on CardioDynamics' BioZ device, which they believe has proven accuracy; and 4) the 2002 TA should have considered abstracts as part of its review, because physicians rely on them. CMS appreciates the input of these beneficiaries and clinicians and has taken their comments into consideration in this coverage review. We address the issues raised in these letters in the CMS Analysis section below.

VI. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally under title XVIII of the Social Security Act §1869(f)(1)(B). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions, no payment may be made for any expenses incurred for items or services that are not "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." §1862(a)(1)(A).

Accuracy of TEB Relative to Other Tests of Hemodynamic Parameters

CMS has thoroughly reviewed all available and relevant literature, including a comprehensive external technology assessment, in order to evaluate the accuracy of TEB. The data provided in these studies suggest that TEB derived hemodynamic measurements generally trend in the same direction as those measures obtained by other, usually invasive, diagnostic testing modalities. In the absence of a universally accepted "gold standard" for the accuracy of hemodynamic parameters, however, it is not possible to make a scientifically supportable determination as to the relative accuracy of TEB compared to any other form of testing. The design and measurement problems found in the available medical literature that prevent such a conclusion from being made at this time are detailed elsewhere in this memorandum. Moreover, because these studies generally included seriously ill patients being treated in the inpatient setting, it would be difficult to generalize these data to TEB use in the ambulatory setting.

Reconsideration of Existing Medicare Coverage

CMS was asked to reconsider the current Medicare coverage policy for TEB due to questions concerning the accuracy, reliability, and clinical utility of the device in addition to the fact that some of the indications for use were non-specific (e.g., suspected or known cardiovascular disease) and some appeared to have little current clinical use (e.g., post heart transplant myocardial biopsy and optimization of atrioventricular interval for patients with A/V sequential pacemaker). CMS sought assistance in performing a literature review from AHRQ in the form of an update to the AHCPR technology assessment that had been published in 1992. Current professional organization guidelines also were reviewed for indications and recommendations on TEB and the results of that review are detailed in an earlier section of this memorandum. In addition, CMS staff searched recent literature, with particular emphasis on studies conducted in 1997 and later, when more technically advanced computer programming was introduced in TEB technology. Of all the studies reviewed, only one included data that would allow for assessment of the impact of TEB on clinical outcomes or in patient management (see below) and that was not for one of the conditions presently covered.

CMS received comments from parties interested in this reconsideration that questioned inclusion of data on the accuracy of hemodynamic measurements obtained by TEB which came from studies performed on antecedent versions of current TEB devices. However, these studies were the basis of CMS' 1998 positive national coverage determination and advocates of both continued and expanded coverage of TEB continue to rely on that data to support their positions on TEB coverage. At the specific request of its manufacturer, CardioDynamics, CMS did evaluate separately the studies using BioZ, in an effort to determine if they showed superiority of that device. That evaluation did not alter the conclusions drawn or the policy being issued in this decision memorandum. In addition, CMS searched for evidence that compared BioZ to other TEB devices but was unable to locate any. In the absence of such a comparison, we are unable to determine whether one device might be superior to another in any respect. Manufacturers interested in making a claim of superiority would need to conduct and publish results from a well-constructed study that directly compares devices.

In reconsidering items or services for which CMS has a long-standing positive national coverage policy, CMS generally would not completely remove coverage unless it became aware of evidence suggesting that the item or service might no longer be reasonable and necessary for the diagnosis or treatment of illness or injury. Such additional evidence might include new information showing that an item or service is harmful or ineffective. However, CMS may elect to refine an existing coverage policy by more precisely defining the circumstances under which coverage is or is not provided if it determines that its existing policy is not clear or is broader in scope than is supported by the evidence.

Upon additional review, CMS has concluded that the indication in the 1998 coverage decision for "suspected or known cardiovascular disease" was written too broadly. Current use of TEB suggests that the policy should articulate more clearly the appropriate uses of TEB for purposes of Medicare coverage. Several of the existing indications were not defined sufficiently to be of use in clinical practice, e.g. "patients in need of determination for intravenous inotropic therapy" and "patients with a need for fluid management." As a general rule, based on the literature reviewed and comments received from experts, the need to determine hemodynamic parameters in patients with cardiac disease should be limited to those instances in which a determination of left ventricular function is essential for the diagnosis or management of congestive heart failure.

The American College of Cardiology/American Heart Association 2001 Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult discussed, but did not recommend, routine use of TEB in part because TEB data has not been shown to be more valuable than routine tests, including the physical examination. The guidelines also strongly recommended against *intermittent* inotropic therapy for any reason in an outpatient setting and recommended that *continuous* positive inotropic therapy be used outside the hospital only as part of an overall plan to allow a patient with terminal heart failure to die with comfort at home or to support a patient waiting for a heart transplant.

Our literature review, the two TA's and the ACC/AHA Guidelines suggest the conclusion that TEB should not be considered as part of the routine treatment for congestive heart failure. We were unable to locate other literature to suggest that it would be considered as a standard of care in management of known or suspected cardiovascular disease. However, when a complete patient history, physical examination, and standard assessment tools fail to provide sufficient information for patient management, the treating physician might wish to use TEB as a noninvasive, relatively simple tool to provide further information about the patient's hemodynamic state in order to optimize the medical regimen. It would be reasonable and necessary to use TEB under those circumstances for the situations specified in section *VII Decision* of this memorandum.

Request to Expand Medicare Coverage to Include Management of Hypertension

CMS received a request to evaluate whether to expand current Medicare coverage of TEB to include its use in the outpatient monitoring and management of hypertension. CMS reviewed the only published study that evaluated TEB in the management of patients with hypertension resistant to treatment with two or more antihypertensive medications. A thorough literature search by both NEMC for the 2002 TA and CMS found no other studies relevant to TEB in managing hypertension.[29] The study by Taler et al. (2002) included data on clinical outcomes for 104 patients with drug resistant hypertension. Resistant hypertension was defined in this study as "the failure to control blood pressure to normal levels (<140/90 mm Hg) using multiple antihypertensive medications [2 medications], including a diuretic." The Seventh Report of the Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, released May 2003 describes resistant hypertension as "the failure to achieve to reach goal BP in patients who are adhering to full doses of an appropriate three-drug regimen that includes a diuretic". [30] CMS will use the JNC diagnosis. All other treatable causes of hypertension, which would prevent response to usual treatment (e.g., renal disease), should have been ruled-out and the treating physician should have assessed patient compliance with previously prescribed treatment before concluding the patient's hypertension is resistant or drug resistant.

The Taler et al. study is a relatively well-designed trial that suggests that TEB may be helpful in patients with drug resistant hypertension who are being treated by a hypertension specialist. The results at the end of 90 days demonstrated a statistically significant, although small, improvement in blood pressure in patients treated using TEB-derived data as compared to a control group treated without TEB. However, the study had some limitations, including:

a) lack of information about randomization and the possibility of bias in patient selection;
b) failure to assess compliance as a cause of differences in study results;
c) use of a treatment algorithm in the experimental arm introducing a second variable to confound results;
d) medication changes made so frequently that it is unclear that drugs reached therapeutic levels before being changed again[31] and;
e) increased diuretic use [32] which could have accounted for blood pressure improvement.

VII. Decision

Based on our review of the evidence as a whole, the previous coverage decision, and in light of the general absence of studies evaluating the impact of using TEB for managing patients with cardiac disease, we conclude that TEB continues to be reasonable and necessary for the following indications with minor modifications to meet the current literature and guidelines:

- Differentiation of cardiogenic from pulmonary causes of acute dyspnea when physician history, physical examination, and standard assessment tools provide insufficient information and the treating physician has determined that TEB hemodynamic data are necessary for appropriate management of the patient;
- Optimization of atrioventricular interval for patients with an atrioventricular sequential pacemaker when physician history, physical examination, and standard assessment tools provide insufficient information and the treating physician has determined that TEB hemodynamic data are necessary for appropriate management of the patient; and
- Monitoring of *continuous* inotropic therapy for patients with terminal congestive heart failure, when those patients have chosen to die with comfort at home, or in patients waiting at home for a heart transplant;
- Evaluation for rejection in patients with a heart transplant as a predetermined alternative to a myocardial biopsy. Medical necessity would need to be documented should a biopsy be performed after TEB.
- Optimization of fluid management in patients with congestive heart failure when physician history, physical examination, and standard assessment tools provide insufficient information and the treating physician has determined that TEB hemodynamic data are necessary for appropriate management of the patient;

Under our original national policy, coverage of TEB for the management of hypertension could have been inferred under the broad category of “suspected or known cardiovascular disease,” and therefore, discretionarily covered by some Medicare contractors if so interpreted. No evidence to support this use was presented in connection with the original coverage decision and it was not our intent to cover management of hypertension at that time. That hypertension was not covered in the earlier decision is supported by the fact that we have now been asked to make a specific coverage determination on TEB for this purpose. Because our intent in this regard may have been unclear in the original decision, any claims that were processed for this purpose under contractor discretion will not be re-examined.

The new evidence reviewed by CMS pertains only to patients with drug resistant hypertension. While the totality of the evidence is not sufficient to support a broad positive coverage determination for this use, it indicates that there may be situations in which TEB could be useful in monitoring of response to medication changes in treatment of drug resistant hypertension. Therefore,

- CMS determines that the coverage and description of the specifics of the situation in which TEB is reasonable and necessary for the treatment of drug resistant hypertension is left to carrier discretion.

Drug resistant hypertension is defined as failure to achieve goal BP in patients who are adhering to full doses of an appropriate three-drug regimen that includes a diuretic.

- CMS also determines that the evidence is inadequate to conclude that TEB is reasonable and necessary for the management of all other forms of hypertension, and therefore its use for all other forms of hypertension is non-covered.

CMS found no evidence to support removing the noncoverage restrictions listed in the current national coverage policy. Therefore, TEB continues to be non-covered when used for monitoring of patients with:

- Proven or suspected disease involving severe regurgitation of the aorta;
- Minute ventilation (MV) sensor function pacemakers, since the device may adversely affect the functioning of that type of pacemaker; or
- During cardiac bypass surgery.

Due to an absence of evidence, all other uses of TEB not described in this memorandum are noncovered.

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1 Bernard G et al., 2000

2 Listening to the chest with a stethoscope to detect abnormal heart and /or lung sounds that may aid in the diagnosis of illness or injury involving these organs.

3 Pulmonary capillary wedge pressure is an indication of left ventricular end diastolic volume. Pressure measurements and oxygen saturation permit the detection of shunting. The pulmonary artery occlusive pressure is useful in assessing left ventricular filling pressure and intravascular volume. Thermodilution is discussed in some detail later in this memorandum.

4 Mueller et al., 1998

5 De Maria A et al., 2000

6 Popp et al., 1990

7 De Maria A et al., 2000

8 Tsadok S, 1999

9 Critchley L, 1998

10 Impedance can be defined as the resistance to the flow of an electrical current. The converse of impedance is conduction.

11 Von Rueden K et al., 1999

12 Cardiac Output = Stroke Volume x Heart Rate

13 Von Reuden K et al, 1999. The authors define these terms as follows: 1) systemic vascular resistance: “afterload, resistance to left ventricular ejection”; 2) change in impedence over time: “magnitude and rate of impedance change, direct reflection of force of left ventricular contraction”; 3) pre-ejection period: “systolic time interval measuring length of time for isovolumetric contraction, Q wave to opening of aortic valve”; 4) ventricular ejection time: “systolic time interval, measuring the length of time for left ventricular ejection, opening to closing of aortic valve”; 5) acceleration contractility index: “direct reflection of left ventricular contractility, calculated from rate of change of blood flow and peak acceleration in ascending aorta”; 6) left cardiac work index: “reflection of myocardial oxygen demand”; and 7) thoracic fluid status: “base thoracic impedance, primarily reflects interstitial, alveolar and intracellular fluid”.

14 De Maria A et al., 2000.

15 This process permits a device manufacturer to market its product on the basis of the device being substantially equivalent to a predicate device.

16 Class II devices are those for which general regulatory controls alone are insufficient to assure safety and effectiveness, but existing methods are available to provide such assurances. (*see* 60 FR48417)

17 Impedance plethysmography is a method of determining changing tissue volumes in the body, based on the measurement of electric impedance at the body surface.

18 Handelsman H, 1992

19 Jordan H et al., 2002

20 Now the Agency for Healthcare Research and Quality (AHRQ).

21 Shoemaker WC et al., 2001

22 ARDS is a condition characterized by acute respiratory failure due to pulmonary edema (fluid in the lungs) caused by increased permeability of the alveolar capillary barrier (the connection between the smallest blood vessels and the air spaces in the lungs).

23 Weinhold et al., 1993

24 Taler S et al., 2002.

25 A sympathetic agonist is an agent, such as a drug, that stimulates the sympathetic nervous system.

26 We do not provide additional details because the study has not yet been published.

27 Hunt et al., 2001

28 Gregoratos et al., 1998

29 One commenter stated that a study by Sramek (1996) had been published. However, other than a cursory summary of the findings, the published article did not provide details about this clinical trial.

30 National Institutes of Health Publication No. 03-5233, 2003

31 The British Hypertension Society recommends that patients should be observed for at least four weeks when a medication is added or a dosage changed to observe the full response to the change before making further changes in medications or dosage, unless there is a need to lower blood pressure more urgently.

32 A recently published study from the Antihypertensive and Lipid-Lowering treatment to Prevent Heart Attack Trial (ALLHAT) supports equal or better blood pressure control with the use of diuretics as compared to other drug antihypertensive therapies.

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Also see subsequent reference list below from the NEMC 2002 Technology Assessment.

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